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Review article

# Systemic lupus erythematosus

*Lupus Eritematoso Sistémico*

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## Abstract

**Introduction:** Systemic lupus erythematosus (SLE) is a pathology of unknown etiology, characterized by chronic activation of the immune system, which generates pathogenic antibodies whose effect will trigger a constant inflammatory state, complicating the clinical picture of the patient. **Materials and methods:** the present descriptive bibliographic review aims to compile the most recent data regarding the disease for its future application as general practitioners, searching information in databases such as PubMed, Medscape, Elsevier, among others. **Results:** Several articles were obtained from the search, however, those that exclusively explored complications of the disease, prevention of superinfections, and not lupus itself were discarded. **Conclusion:** Thanks to advances in diagnostic methods and therapy for SLE, it has been possible to reduce mortality and the potential of the disease to generate disability.

**Keywords:** Systemic Lupus Erythematosus, Antigen-Antibody Complex, Biological Therapy, Inflammation, Connective Tissue.

## Resumen

**Introducción:** El lupus eritematoso sistémico (LES) es una patología de etiología desconocida, caracterizado por la activación crónica del sistema inmunitario, el cual genera anticuerpos patógenos cuyo efecto desencadenará un constante estado inflamatorio, complicando el cuadro clínico del paciente. **Materiales y métodos:** la presente revisión bibliográfica de tipo descriptiva tiene como objetivo compilar los datos más recientes respecto a la enfermedad para su futura aplicación como médicos generales, efectuando la búsqueda información en bases de datos como PubMed, Medscape, Elsevier, entre otras. **Resultados:** Se obtuvieron de la búsqueda varios artículos, sin embargo, se descartaron aquellos que exploraban exclusivamente complicaciones de la enfermedad, prevención de sobreinfecciones, y no el lupus en sí. **Conclusión:** Gracias al avance en métodos diagnósticos y la terapéutica del LES se ha logrado reducir la mortalidad y el potencial de la enfermedad para generar discapacidad.

**Palabras clave:** Lupus Eritematoso Sistémico, Complejo Antígeno-Anticuerpo, Terapia Biológica, Inflamación, Tejido Conectivo.

## Introduction

Systemic lupus erythematosus (SLE) is considered a prototypical autoimmune systemic disease, characterized by chronic and recurrent activation of the immune system due to the production of antibodies against nuclear and cytoplasmic antigens, causing multisystemic inflammation. It is predominant in women (90% of cases), it usually appears from the fertile age; However, the possibility of presentation in men is not excluded, having a greater predilection for Afro-descendant, Hispanic and Asian patients; the age of presentation varies and is directly proportional to the prognosis of the disease; These irregularities in the function of the immune system cause it to affect and endanger the health of the patient, hence the importance of reviewing this disease [1-4].

## Methodology

The general objective of this descriptive review is to compile recent information regarding the disease, through a methodological search, at the same time as old texts that deserve to be referenced due to their historical content will be added, in order that this manuscript constitutes a tool reminder about SLE, for general practitioners and Health Sciences students. Specifically, the emphasis will be on summarizing the known and up-to-date data on the pathology; suggest the diagnostic technique or criteria and the therapeutic options according to the available clinical practice guidelines.

In November 2019, a search was carried out in PubMed with the MESH terms "Systemic lupus erythematosus", "adults" linked by the Boolean operator AND, and the MESH term "pregnancy" preceded by the Boolean operator NOT, applying the language filters (English), type of articles (review articles), free full text, species (humans) and time interval (5 years).

## Results

A total of 10 results were obtained; however, those that explored complications of the disease (such as lupus nephritis, vision loss, chronic fatigue, etc.) or for its management (vaccination) and not lupus itself, or that referred to rheumatological diseases in general, throwing at the end a total of 3 selected.

To the results obtained from the methodological search, the information was supplemented by reviewing the clinical practice guidelines for systemic lupus erythematosus of Spain, together with the clinical practice guidelines for lupus from the Ministry of Public Health of Ecuador, to Obtain data on current therapeutic attitudes towards the disease.

Additional books were consulted to add data on the etiopathogenesis and clinical manifestations; In addition, Medscape was consulted to incorporate information in this regard, Elsevier and PubMed publications were also reviewed, as well as bibliographies that exceed 5 years old, for the incorporation of historical data regarding the disease, which have not been published. Been the subject of investigation at the current dates, but that its contemplation for the review was necessary.

## Development

The term "lupus", from the Latin meaning wolf, corresponds to a chronic inflammatory autoimmune disease, with a wide range of clinical manifestations because of its systemic effect on multiple organs [1-13]. It was allegedly discovered by Hippocrates in the 5th century BC. de C., who used the term herpes sthiomenos (persistent dermatosis) to refer to lesions. This is how, in 855, it is mentioned that Herbernus, Archbishop of Tours, used the term lupus for the

first time to refer to this type of skin lesion [14, 15, 16].

For many years the term continued to be used to refer to skin lesions; Rudolph Virchow linked all processes with ulceration and necrosis of the lower extremities within the concept of lupus; however, the description of the disease as such was still incomplete [15]. Laurent Theodore Biett exposes the first clear description of the disease as such, coining the term erythema centrifugum and later his student Louis Alphée Cazenave refers to it as lupus erythematosus, making allusion to a rare condition that mainly affected the female sex, characterized by raised reddened lesions the size of a coin with a prominent edge and whose center returned to normal color, which could spread to a large part of the face [15, 17].

### *Ethiopathogenesis*

The etiopathogenesis of SLE is still not fully understood, however, there are many mechanisms related to the development of the disease; studies in the human genome reveal the predisposition to SLE, manifested by an inadequate response of the immune system, mediated by the interruption in lymphocytic signaling, interferon response, complement elimination, apoptosis, DNA methylation; It is worth mentioning that there are processes such as oxidative stress in the mitochondria in which short fragments of DNA (mitochondrial DNA) are produced that can manifest as lupus-like diseases [3,5,7,23]; the characteristic genetic dysfunction and error in T cell signaling have been related to genes such as PTPN22, TNFSF4, PDCD1, IL10, BCL6, IL16, TYK2, PRL, STAT4 and RASGRP3, processing of immune complexes and innate immunity, including the presence of complementary genes (C2, C4A and C4B); however, environmental factors such as solar radiation, viral infections, vitamin D deficiency, among others, are necessary to be able to manifest the disease [3, 5-7].

The presence of pathogenic antibodies is another crucial determinant for the manifestation and course of the disease, including B cells and plasma cells; However, based on studies, a central role can be attributed to T cells, which, due to defects in both signaling (favoring the entry of calcium, possibly due to changes in the CD3 signaling subunits) and in the effector function (secreting less interleukin-2 (IL-2), affecting migration, adherence and aid of B cells, T-regulatory and cytotoxicity of CD8) [3, 5-7].

### *Clinical manifestations*

The clinical manifestations that lead the disease are the general ones, the main ones being fever, asthenia and weight loss with frequency of 90 to 95% of the cases, followed by mucocutaneous involvement (such as malar rash, alopecia, mucous ulcers, discordant lesions) and musculoskeletal involvement (arthritis, arthralgia, avascular necrosis, myositis, among others) with a frequency of 80-90%, in both types; 50-70% of cases will present serositis, 40-60% glomerulonephritis or neuropsychiatric involvement, and 20-30% autoimmune cytopenia [1].

The appearance of symptoms can occur in recurrent episodes followed by phases of remission, among the most common manifestations, we have erythema in butterfly wings, (red rash on the nose and cheeks after sun exposure), alopecia, Raynaud's phenomenon and canker sores in the mouth or nose; Regarding respiratory manifestations, the appearance of painful breathing, cough and dyspnea, pleural effusion and pulmonary hypertension have been reported; cardiovascular effects often include pericarditis, myocarditis, endocarditis, and coronary artery disease; gastrointestinal involvement includes nausea, vomiting, and abdominal pain; reported hematologic changes include anemia, as well as leukopenia or thrombocytopenia [2, 19].

### *Diagnosis*

In 2019, the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) released an update regarding the diagnostic criteria for SLE. And it is that this disease is considered a challenge for its diagnosis. This disease is characterized by heterogeneous manifestations, with a variable clinical course, many of its tests are not entirely specific, and the fact that it is a pathology that shares clinical manifestations with many diseases makes it difficult to diagnose SLE.

The guide for clinical practice of SLE of the Ministry of Public Health of Ecuador (MSP) based on the forms of initiation of SLE indicates that

"A patient can first go to a general practitioner, primary care, family doctor or another of any discipline or specialty, in addition, at some point in their evolution, the patient may need the participation of any of them"; Thus, the role of the general practitioner can occur in two different contexts, in the stable patient

(without symptoms of severe active disease), in which case it should be derived by normal flow; and the unstable patient (with signs of severe active disease), in whom a prompt evaluation by the rheumatologist should be managed in the consultation or by referral to the emergency room, direct hospitalization 8. The initial criterion for diagnosis is the presence of antinuclear antibodies (ANA) ≥1: 80 in HEp-2 cells or equivalent positive test at least once. Immunofluorescence testing on HEp-2 cells or solid phase ANA immunoassay with at least equivalent performance is recommended. The criteria are grouped into 7 clinical domains and 3 immunological domains.

**Table 1.** Definition and criteria of the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) for the classification of systemic lupus erythematosus 12, 24.

| Clinical criteria | Definition | Score |
|---|---|---|
| Fever | Temperature> 38.3 ° C | 2 |
| Leukopenia | White blood cell count <4,000 / mm3. | 3 |
| Thrombocytopenia | Platelet count <100,000 / mm3. | 4 |
| Autoimmune hemolysis | Evidence of hemolysis, such as reticulocytosis, low haptoglobin, elevated indirect bilirubin, elevated LDH, and a positive Coombs test (direct antiglobulin). | 4 |
| Delirium | Characterized by 1) change in consciousness or level of arousal with reduced ability to concentrate, 2) development of symptoms over hours to <2 days, 3) fluctuation of symptoms throughout the day, 4) either 4a) acute / subacute change in cognition (eg, memory deficit or disorientation), or 4b) change in behavior, mood, or affect (eg, restlessness, reversal of the sleep / wake cycle). | 2 |
| Psychosis | Characterized by 1) delusions and / or hallucinations without insight and 2) absence of delirium. | 3 |
| Seizures | Primary generalized attack or partial / focal attack. | 5 |
| Alopecia without scars | Non-scarring alopecia observed by a clinician. | 2 |
| Oral ulcer | Oral ulcers observed by a clinician. | 2 |
| Subacute or discoid utaneous lupus | Physician-observed subacute cutaneous lupus erythematosus: † Annular or papulosquamous (psoriasiform) skin rash, usually photodistributed. If a skin biopsy is performed, typical changes should be present (vacuolar interface dermatitis consisting of a perivascular lymphohistiocytic infiltrate, often with dermal mucin observed discoid lupus erythematosus observed by a physician: † | 4 |
| Acute cutaneous lupus | Erythematous-violaceous skin lesions with secondary changes of atrophic scarring, depigmentation, often follicular (scalp) hyperkeratosis / plugging, leading to scarring of the scalp. If a skin biopsy is performed, typical changes present should be made (vacuolar interface dermatitis, consisting of a perivascular and / or periappendageal lymphohistiocytic infiltrate). Keratin follicular plugs may be seen on the scalp. In long-term lesions, a deposit of mucin may be seen. | 6 |
| Pleural or pericardial effusion | Imaging evidence (such as ultrasound, X-ray, CT scan, MRI) of pleural or pericardial effusion or both. | 5 |
| Acute pericarditis | ≥2 of 1) pericardial chest pain (typically acute, worse on inspiration, improved when bending forward), 2) pericardial rub, 3) electrocardiogram with new generalized ST elevation or PR depression, 4) new or worse pericardial effusion in the images (such as ultrasound, X-ray, CT scan, MRI). | 6 |
| Joint involvement | Either 1) synovitis involving 2 or more joints characterized by swelling or effusion OR 2) tenderness in 2 or more joints and at least 30 minutes of morning stiffness. | 6 |
| Proteinuria | Proteinuria> 0.5 g / 24 hours per 24-hour urine or an equivalent ratio of protein to creatinine in point urine. | |

| | | |
|---|---|---|
| Class II or V lupus nephritis in biopsy according to ISN / RPS 2003 classification | Class II: mesangial proliferative lupus nephritis: purely mesangial hypercellularity of any degree or renal expansion of the mesangial matrix by light microscopy, with mesangial immune deposit. Some isolated subepithelial or subendothelial deposits may be visible by immunofluorescence or electron microscopy, but not by light microscopy. Class V: membranous lupus nephritis: global or segmental subepithelial immune deposits or their morphological sequelae by light microscopy and by immunofluorescence or electron microscopy, with or without mesangial alterations. | 8 |
| | Class III: focal lupus nephritis: active or inactive focal, segmental or global endocapillary or extracapillary glomerulonephritis involving <50% of all glomeruli, typically with focal sub-endothelial immune deposits, with or without mesangial abnormalities.<br><br>Class IV: diffuse lupus nephritis: diffuse endocapillary or extracapillary glomerulonephritis, segmental or global active or inactive involving ≥50% of all glomeruli, typically with diffuse subendothelial immune deposits, with or without mesangial alterations. This class includes cases with diffuse wire loop deposits, but little or no glomerular proliferation.<br><br>Class V: membranous lupus nephritis: global or segmental subepithelial immune deposits or their morphological sequelae by light microscopy and by immunofluorescence or electron microscopy, with or without mesangial alterations. | 10 |
| Positive antiphospholipid antibody | Medium or high titer anticardiolipin antibodies (IgA, IgG or IgM) (> 40 APL, GPL or MPL, or> 99th percentile) or positive anti-β2GPI antibodies (IgA, IgG or IgM) or positive anticoagulant for lupus. | 2 |

| Immunological criteria | Definition | Score |
|---|---|---|
| C3 or C4 low | C3 OR C4 below the lower limit of normal. | 3 |
| C3 and C4 low | Both C3 and C4 are below their lower limits of normal. | 4 |
| Anti-dsDNA antibodies or anti-Sm antibody | Anti-dsDNA antibodies in an immunoassay with demonstrated ≥90% specificity for SLE against relevant disease controls OR anti-Sm antibodies. | 6 |
| Positive antiphospholipid antibody | Medium or high titer anticardiolipin antibodies (IgA, IgG or IgM) (> 40 APL, GPL or MPL, or> 99th percentile) or positive anti-β2GPI antibodies (IgA, IgG or IgM) or positive anticoagulant for lupus. | 2 |

**Table 2.Autoantibodies and clinical significance in systemic lupus erythematosus 2.**

| Autoantibody | Clinical associations |
|---|---|
| Anti-dcDNA | 95% specificity in SLE; fluctuates with disease activity; associated with glomerulonephritis. |
| Anti-smith | 99% specificity of SLE; associated with anti-U1RNP antibodies. |
| Anti-U1RNP | Antibody associated with mixed connective tissue disease and less frequent glomerulonephritis. |
| Anti-Ro / SS-A | Associated with Sjögren's syndrome, photosensitivity, LECS, neonatal lupus, congenital heart block. |
| Anti-La / SS-B | Associated with Sjögren's syndrome, LECS, neonatal lupus, congenital heart block, anti-ro / SS-A. |

Of these, the detection of antinuclear antibodies (ANA) stands out, which is not specific for the diagnosis of lupus, but which gives the examining physician an important diagnostic orientation and although it is true there are reports of cases of SLE with negative ANA, its absence may be useful when ruling out the possibility of suffering from SLE 2. The detection of anti-dsDNA antibodies, on the contrary, is a highly specific test; its presence can provide a confirmatory diagnosis for SLE; however, it is a test that takes longer than the detection of ANA and whose absence does not rule out the possibility of suffering from the disease.

Other antibodies are also taken into account, which are not strictly specific for the detection of SLE, but which can serve as an indicator of other pathological processes such as neonatal lupus, Sjögren's syndrome or subacute cutaneous lupus erythematosus (SLE), which gives a great contribution to the definitive and differential diagnosis of the disease [2, 8, 9]. The aforementioned antibodies, together with their link with SLE, and part of their differential diagnoses are detailed in Table 2.

As it is a pathology of wide manifestation and sometimes nonspecific, many disorders can simulate the disease, among which patients with parvovirus B19 stand out, which manifest as a rash, systemic inflammatory polyarthritis fever and cytopenias; even positivity for ANA and anti-dcDNA and hypocomplementemia are also related. In the same way, exposure to viral agents such as the Epstein Barr virus (EBV), hepatitis B and C viruses, cytomegalovirus, and the suffering of some neoplasms such as lymphomas, as is the case of Hodgkin's disease, which is Characterized by joint pain, cytopenias, lymphadenopathy, rash, positive and harmful ANA, they are considered within the table of differentials, due to their nonspecific symptomatological picture [2, 8].

Another important factor to consider is neonatal lupus, caused by the transmission of anti-SSA or anti-SSB antibodies from the mother, this condition is counterproductive for the product that due to the activity of these antibodies can suffer complications of variable severity, Among these complications, one of the most pronounced is complete congenital heart block and cardiomyopathy.

### *Therapy*

The general consultation will proceed to the treatment of symptoms and adverse events of the drugs, stabilization and / or referral. The MSP medical practice guide for the management of SLE sets out a therapeutic algorithm that emphasizes the appropriate attitude of the general practitioner when faced with the suspicion or confirmation of diagnosis of SLE, which is detailed in flowchart [1 8].

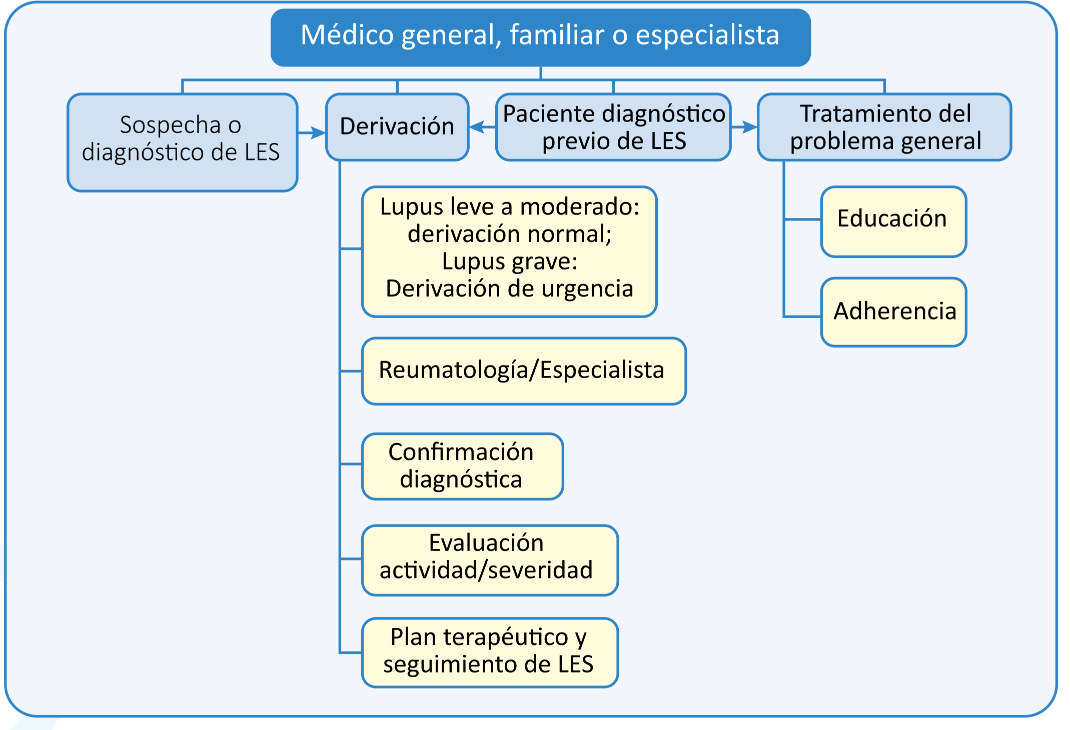



***Figure 1.*** *Flowchart "Medical Role in SLE care". Role of the non-specialist doctor in coping with a patient with SLE, taken from the MSP 8 clinical practice guide.*

**Table 3. Drugs used in the recommended pharmacological control of systemic lupus erythematosus 10.**

| Drug | Dose | Dose adjustment | Toxicity requiring vigilance | Baseline assessment | Laboratory surveillance |
|---|---|---|---|---|---|
| **Azathioprine** | 50-200 mg / day; 1-3 doses with food | ↓ 25% eGFR (glomerular filtration) 10-30 ml / min; ↓ 50% if eGFR <10 ml / min | Myelosuppression, hepatotoxicity, lymphoproliferative disease | Hemoglobin, platelets, creatinine (Cr), Aspartate transaminase (AST) OR Alanine transaminase (ALT) | Hemoglobin and platelet every 2 weeks, with changes in dose; baseline tests every 1-3 months |
| **Mycophenolate mofetil** | 1-3 g / day; in divided doses with food | Maximum 1g / day if eGFR <25 ml / min | Myelosuppression, hepatotoxicity, infection | Hemoglobin, platelets, Cr, AST, or ALT | Hemoglobin and platelets every 1-2 weeks with dose changes; baseline tests every 1-3 months |
| **Cyclophosphamide** | 50-150 mg / day in a single dose with breakfast. Increase your fluid intake (at least 3L and water / day), empty your bladder before going to bed * | ↓ 25% if eGFR 25-50 l / min; ↓ 30-50% if eGFR <25 ml / min; ↓ 25% if there is liver dysfunction (serum bilirubin 3.1-5 mg / dl or transaminases> 3 times the upper limit of normal (ULN)) | Myelosuppression, hemorrhagic cystitis, myeloproliferative disease, malignant neoplasms | Hemoglobin, platelets, Cr, AST, or ALT, urinalysis | Hemoglobin with differential every 1-2 weeks, with changes in dose, and then every 1-3 months; maintain leukocytes> 4000 / mm3 with dose adjustment; urinalysis, AST or ALT every 3 months; urinalysis every 6-12 months after cessation |
| **Methotrexate** | 7.5-25 mg / week in 1-3 doses with food or milk / water | ↓ 50% if eGFR 10-50 ml / min; avoid use if eGFR <10 ml / min; avoid use in liver dysfunction | Myelosuppression, liver fibrosis, pneumonitis | Chest X-ray (CXR), hepatitis B / C serology in high-risk patients, AST or ALT, albumin (Alb), alkaline phosphatase (FA), Cr | Hemoglobin with platelets, AST, Alb, Cr every 1-3 months |
| **Cyclosporin A** | 100-400 mg / day in two doses at the same time each day with or between meals | Avoid impaired kidney function | Kidney failure, anemia, hypertension | Hemoglobin, Cr, uric acid, ASTo ALT, Alb, FA, blood pressure | Cr every 2 weeks until stable dose, then monthly; hemoglobin, potassium, AST or ALT, Alb and FA every 1-3 months; drug concentrations only at doses> 3 mg / kg / day |
| **Tacrolimus** | 1-4 mg / day in two doses at the same time each day | Prudent use in liver or kidney failure | Renal failure, neurotoxicity, malignancies, infections, hyperkalemia | Cr, potassium, ASTo ALT, glucose, blood pressure | Baseline tests once a week for the first 3-4 weeks. Then every 1-3 months; monitor trough drug concentrations |
| **Leflunomide** | *100 mg / day in a single dose for 3 days. After 10-20 mg / day* | *Avoid liver dysfunction* | *Myelosuppression, hepatotoxicity, fetal toxicity* | *Hemoglobin, Cr, AST or ALT, Alb, FA* | *Hemoglobin, AST or ALT, Alb, and FA monthly for 6 months, then every 1-3 months; monthly monitoring if MTX is administered* |

SLE is a disease with a prognosis that is directly dependent on comorbidities, the patient's risk factors, and the time for diagnosis and an adequate therapeutic plan, so setting an attitude to follow as soon as possible becomes one of the main objectives. for its management; In the clinical practice guidelines for the management of SLE it is emphasized that in the presence of a definitive or presumptive diagnosis of SLE, the role of the general practitioner is to proceed with the referral so that the case is managed by the specialist doctor, who in this case It is the responsibility of the rheumatologist, who will confirm the diagnosis of the disease, assess its activity and severity, and proceed with the designation of a therapeutic plan [8].

As it is a systemic pathology, its pharmacological therapy will be oriented to the disease, stage and concomitants, so that in mild to moderate stages the use of low doses of corticosteroids, antimalarials or methotrexate is justified and recommended, while in advanced stages and severe patients, it is recommended to start with high doses of corticosteroids, hydroxychloroquine and immunosuppressive therapy, such as the use of cyclophosphamide, azathioprine or mycophenolate mofetil, the drugs together with their respective doses are detailed in Table 3.

For cases of SLE in children, management should follow a multidisciplinary approach, and the diagnosis should be made as soon as possible; Although it is true, it is not contraindicated, the guidelines recommend evaluating the state of the disease before planning a pregnancy, and in case of presenting active disease, the use of hydroxychloroquine, prednisone and aspirin is recommended as treatment alternatives, and should avoid the use of immunosuppressants such as azathioprine and cyclophosphamide [8].

Studies are currently being carried out to try to incorporate biological therapy with the aim of having more therapeutic options, such as Ocrelizumab, Epratuzumab, Abatacept, the use of interferon and anti-interleukin [6] inhibitors, which will seek to offer the patient patient a better quality of life [10]. Thus we also have agents that are used in addition

to the usual ones such as Belimumab, which is applied in cases of SLE resistant to more than one of the established therapeutic regimens, as long as it is SLE without kidney involvement [25].

## Discussion

SLE is a pathology of variable presentation and difficult to diagnose; however, detecting it early can help patients improve their quality of life and prevent a dire outcome; This is the reason why the clinical practice guidelines for the management of SLE emphasize both the use of diagnostic techniques, in which the general practitioner or treating physician, based on the clinical picture, history and serological tests can make the early diagnosis and referral to the specialist at the appropriate time [8, 9].

Despite emphasizing, in the reviewed literature, that the detection of ANA is not a test with high specificity for SLE, this is still a necessary test for its diagnosis, for this reason it must be requested by the primary care physician. and in the case of detecting positivity, perform specific antigen tests, such as those focused on double-stranded DNA (dsDNA) or ribonucleoprotein complexes (Ro / SSA, La / SSB, Smith and RNP), however, despite Considering the specificity of some such as anti-dsDNA (> 60%) or anti-Smith (90%), it should be noted that these are usually detected in a limited percentage of patients (anti-Smith 30%) [26]; detection of anti-dsDNA is late; however, specific to LES, for this reason, and despite delaying its detection in the diagnostic procedure as stated in the European guideline, in the event of a positive ANA, the evaluation of anti-dDDNA is supported; Regarding serological tests, the use of the human epithelial cell line (HEp2 cell line) has been commented and the European guide exposes the existence of several serological tests that provide similar results; however, the current evidence is not sufficient to support them [2, 8, 9].

Regarding its treatment, the guidelines recommend starting with antimalarial, because drugs such as cyclophosphamide, azathioprine or the use of glucocorticoids increase the risk of adverse reactions and, consequently, the appearance of fatal complications in patients; Immunosuppressive therapy is not recommended as a first option, unless tolerated by the patient; Hydroxychloroquine is considered one of the first-line drugs in SLE, however, more advances are expected in relation to its therapeutics, such as the use of biological therapy; Likewise, it is essential to educate the patient and give a preventive approach to the disease in order to be able to provide it with a better quality of life [8, 9, 10].

Anifrolumab is a fully human monoclonal antibody, it acts by binding to subunit 1 of the IFN type I receptor (IFNAR1), blocking the action of different IFN type I (IFN-α, IFN-β and IFN-ω), in adults with moderate to severe SLE (MUSE trial) it showed positive results; observing greater efficacy in patients with a high signature compared to those with a low signature of the baseline IFN gene; With regard to studies on the prognosis of the disease, the clinical results after treatment with rituximab (RTX) in patients with SLE are highly variable, in the study by Pirone et al. a low to very low quality of evidence was determined according to the GRADE scale, concluding that “studies that address prognostic factors generate hypotheses and cannot be used to make specific recommendations for routine clinical practice”; the measurement of disease activity is essential for clinical research, assessing the clinical status of the patient with SLE is the central question regarding its management, especially with the failure of clinical trials of biological therapy; The treatment aims to improve the state of the disease or lessen its deterioration, exacerbations, and improve the quality of life of patients, and this becomes difficult with the absence of a gold standard to measure the level of improvement or the severity of the disease outbreak (especially on a biomarker-based standard);

## *Conclusion*

Despite the large number of studies on SLE, much remains to be investigated, especially in the diagnostic and therapeutic fields; lupus can appear at any age, and its aggressiveness will depend on its chronicity; The detection of positive ANA is an important indicator and diagnostic guide, however, as it is not specific for SLE, it is recommended to carry out other tests focused on the detection of anti-dsDNA.

SLE is a pathology with systemic manifestations, its therapy should focus on the control of the disease and the treatment of its concomitants.

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